REMARKS/ARGUMENTS

The July 29, 2003 Office Action has rejected all pending claims under 35 U.S.C. § 103(a) as being unpatentable over Karron, et al. in view of Wu, et al. and further in view Sninsky.

Applicants' attorney telephonically interviewed Examiner Siew on Friday, October 3, 2003. Applicants and their attorney thank Examiner Siew for the courtesy of his time and for his helpful suggestions.

During the interview, Applicants noted that the Wu, et al. disclosure is not drawn to a demonstration of the efficacy of multiple targets and unequal primer concentrations. Applicants' attorney and Examiner Siew agreed that Applicants would present claims with the limitation of claim 35 as part of current claim 34. Applicants have done that. Applicants will also file a continuation case taking advantage of the Examiner's suggestion to focus on particular target nucleic acids.

Applicants note that the Wu reference teaches and describes the process of making an asymmetric PCR. Wu teaches that as part of this method it is optimal to use unequal primer concentrations greater than 5 to 1, but at least 2 to 1. The goal of this teaching is clearly to

make one strand of the PCR reaction the major final product in large (logarithmic) excess compared to the other strand. This is most evident by Wu, et al.'s statements that "Denaturation of the . . . (DNA) products . . . is not needed" (see Wu, et al., page 1, abstract); "After the last cycle of amplification, the product formed with the primer in excess is detected in a suitable manner without the need for a final heating, or denaturation, step" (see Wu, et al., at page 4, line 39); and "Moreover, the enzyme detection reagents are used in combination with an unequal amount of primers in the amplfication procedures so that denaturation prior to detection of the product from the excess primer can be avoided" (see Wu, et al., at page 3, line 16). Wu neither teaches nor suggests that this method would be more efficient (increased sensitivity) for making that one strand over equal molar concentrations of the primers. Wu's goal is to make a single strand of DNA. In contrast, the method of the present invention creates double-stranded DNA as the major species, not single-stranded DNA.

Additionally, Wu does not teach that unequal primer concentrations would be successful for making a multiplex PCR reactions (2 or more targets) with increased yield.

The present invention teaches how to make a multiplex PCR reaction with any group of primers more efficient than a reaction in which primers are mixed in equal molar ratios of 1:1 (5′ to 3′ primers). We have found the ratios expressed in claim 35 to be the most efficient when compared to 1:1 (5′ to 3′). Note claim 37 drawn to at least 3.5 times more product than reactions from primers at equal concentrations.

Amendment of the Title

Applicants have amended the title to more closely reflect the invention.

Applicants believe the claims to be allowable and respectfully request a Notice of Allowance. If further fees are necessary, please charge Deposit Account 17-0055.

Respectfully submitted,

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October 29, 2003 By: Jean C. Baker

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